DNA in 10 nM tris buffer, pH 7.5, and 0.18 M sodium chloride. The variation of the successive autocorrelation functions reveals the kinetics of association. Autocorrelation was determined after 0, 0.5, 1, 2, 4, 8, 16, 32, 64, 128, 192, and 256 minutes. The diffusion time of the free primer is 0.17 ms, and 2.9 ms when complex-bound. Figure 29 shows the course of the association as experimentally revealed as % fraction of the primer in the associated complex. A reassocation rate of 0.07 min^{-1} results.

E2, cond'd

IN THE CLAIMS

Rewrite claim 121 as follows.

~~121~~ (amended). The device according to claim ~~119~~ 1 wherein said pinhole aperture has a diameter of ≤ 100 micrometer.

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Add the following claims.

61 ~~139~~. The device according to claim ~~120~~ 60 wherein said pinhole aperture has a diameter of ≤ 100 micrometer.

62 ~~140~~. The device according to claim ~~120~~ 60 wherein said molecules, molecular complexes or molecular fragments are in a dilution of ≤ 1 micromolar.

E4 contd.

63 ~~141~~. The device according to claim ~~120~~ 60 wherein said measuring volume is ≤ 10^{-14} liter.

64 ~~142~~. The device according to claim ~~120~~ 60 wherein with an image scale of 1:100, 1:60, or 1:40 between the measuring volume and the image plane and with a measuring volume having

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dimensions of ≤ 0.1 micrometer in each direction, said pinhole aperture has a diameter of about 10 micrometer, 6 micrometer, or 4 micrometer, respectively.

65 ~~143.~~ The device according to claim 60 ~~120~~ wherein the focusing device for focusing said laser beam onto said measurement volume has a numerical aperture of ≥ 1.2 N.A.

66 ~~144.~~ The device according to claim 60 ~~120~~ wherein the focusing device has a prefocusing device to prefocus the laser beam and a focusing objective lens to focus the prefocused laser beam onto the measuring volume.

67 ~~145.~~ The device according to claim 66 ~~144~~ wherein the distance between the focusing objective lens and the measuring volume is up to 1,000 micrometer.

68 ~~146.~~ The device according to claim 66 ~~144~~ wherein a semitransparent mirror is arranged between the prefocusing device and the focusing objective lens to deflect the prefocused laser beam on the focusing objective lens.

69 ~~147.~~ The device according to claim 68 ~~146~~ wherein the pinhole aperture is arranged at a side of the semitransparent mirror facing away from the focusing objective lens.

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72 ~~148.~~ The device according to claim 60 ~~120~~ wherein an optic for transmitting the fluorescence radiation has a numerical aperture of ≥ 1.2 N.A.

73 ~~149.~~ The device according to claim 60 ~~120~~ wherein the detector device has one or more detectors for detecting the fluorescence radiation.

74 ~~150.~~ The device according to claim 60 ~~120~~ wherein at least one optical filter is arranged between the pinhole aperture and the detector device.

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75 ~~151~~. The device according to claim 60 ~~120~~ wherein at least one imaging lens is arranged between the pinhole aperture and the detector device.

76 ~~152~~. The device according to claim 60 ~~120~~ wherein at least one semitransparent mirror is arranged between the pinhole aperture and the detector device.

77 ~~153~~. The device according to claim 60 ~~120~~ wherein at least one reflecting mirror is arranged between the pinhole aperture and the detector device.

sub G2

154. The device according to claim 120, further comprising

e) an additional laser beam generation device for generating an additional laser beam with a wavelength different from the first wavelength,

f) an additional focusing device for focusing said additional laser beam onto the measuring volume wherein the additional laser beam is such highly focused within the measuring volume that in essence it exclusively covers the measuring volume,

E4

g) an additional detector device for detecting fluorescence radiation generated due to excitation of one or more molecules, molecular complexes or molecular fragments, and

h) a correlator unit which is connected with the two detector devices.

155. The device according to claim 154, further comprising

i) a T-shaped support with a first supporting arm and a second supporting arm connected therewith and running perpendicular to the first supporting arm,

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j) ~~two holding devices arranged at the ends at the faces of the second supporting arm for axial guiding and holding of optical elements (lens, filter, mirror, detector) for the two laser beams and the two fluorescence radiations wherein the focused laser beams impinge on a glass slide bearing the measuring volume and being separably arranged between the two ends at the faces of the second supporting arm and held by them,~~

~~wherein the two holding devices can be moved synchronously relative to their respective ends at the faces of the second supporting arm in a direction of a longitudinal extension thereof, the two holding devices are extended in a direction of extension of the first supporting arm, and the two laser beams can be deflected by deflecting mirrors through optical openings out of an inside of the first supporting arm onto the optical elements for the laser beams held at the holding devices.~~

156. ~~The device according to claim 154, further comprising~~

E4

i) ~~a T-shaped support with a first supporting arm and a second supporting arm connected therewith and running perpendicular to the first supporting arm,~~

j) ~~two holding devices arranged at the ends at the faces of the second supporting arm for axial guiding and holding of optical elements (lens, filter, mirror, detector) for the two laser beams and the two fluorescence radiations wherein the focused laser beams impinge on a glass slide bearing the measuring volume and being separably arranged between the two ends at the faces of the second supporting arm and held by them,~~

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wherein the two holding devices can be moved synchronously relative to their respective ends at the faces of the second supporting arm in a direction of a longitudinal extension thereof, the two holding devices are extended in a direction of extension of the first supporting arm, and the two laser beams can be deflected by semitransparent mirrors through optical openings out of an inside of the first supporting arm onto the optical elements for the laser beams held at the holding devices.

157. The device according to claim 136 wherein the focused laser beams are being separably arranged halfway between the two ends at the faces of the second supporting arm.

158. The device according to claim 136 wherein the optical elements for the laser beams are arranged at the inner sides, facing each other, of the two holding devices and the optical elements for the fluorescence radiation are arranged at the outer sides, facing away from each other, of the two holding devices.

E4

159. The device according to claim 136 wherein one of the focusing objective lenses can be positioned by an adjusting element for compensation of an offset of the focuses of said focusing objective lenses.

27 ~~160~~. The device according to claim 26 ~~159~~ wherein the adjusting element is piezoelectrically driven.

28 ~~161~~. The device according to claim 1 ~~119~~ wherein the observation unit has photon counting appliances, a correlation appliance, and a multichannel scaler appliance.

sub G3

162. The device according to claim 161 comprising means for processing or evaluating the measuring signal in a computer assisted way.

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163. The device according to claim 126 wherein the appliances for prefocusing are provided with a lens and an array corresponding to microscope optics wherein a colonnaded laser beam is focused on the image plane B_1 by a lens and on the image plane B_2 (first image) by said array.

12 ~~164.~~ The device according to claim 11 ~~163~~ wherein said array is provided with an exchangeable arrangement of lenses for the variation of the diameter of the prefocused laser beam.

30 ~~165.~~ The device according to claim 1 ~~119~~ wherein a detection unit is constituted by two detectors with a beam splitter partitioning the light emitted from the sample to the detectors.

31 ~~166.~~ The device according to claim 30 ~~165~~ wherein the emitted light beam passes imaging lenses and filter elements prior to each of the detectors.

32 ~~167.~~ The device according to claim 30 ~~165~~ wherein the detectors detect light of different wavelengths.

64 168. The device according to claim 119 wherein one or more detector elements are placed in the image plane in the form of a detector array.

sub G4

33 ~~169.~~ The device according to claim 1 ~~119~~ comprising two objectives which form an angle of >90° between them.

sub G5

170. The device according to claim 119 wherein continuous lasers emitting light of wavelengths > 200 nm are used.

171. The device according to claim 170 wherein argon, krypton, helium-neon, or helium-cadmium lasers are used.

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172. The device according to claim 119 wherein lasers pulsed with high frequency of ≥ 20 MHz with a power of ≥ 0.5 mW are used.

37 ~~173.~~ The device according to claim ~~119~~ 1 wherein appliances for single photon counting are arranged in the beam path of emitted light for detecting the emitted light wherein signal analysis is performed by a digital correlator or multichannel correlator.

38 ~~174.~~ The device according to claim ~~173~~ 37 wherein said appliances for single photon counting are avalanche diode detectors.

39 ~~175.~~ The device according to claim ~~173~~ 37 wherein said appliances for single photon counting are arranged in the plane of the pinhole aperture.

40 ~~176.~~ The device according to claim ~~119~~ 1 wherein the measuring volume is situated in a sample volume between two capillaries, said capillaries being provided with a chemically inert conductive coating at the outer side, and wherein the conductive coatings are connected via a computer controlled rectified field or an alternating field and are conductively connected with each other through the measuring volume.

E4

41 ~~177.~~ The device according to claim ~~176~~ 40 wherein the coating is a metal vapor deposited coating.

42 ~~178.~~ The device according to claim ~~177~~ 41 wherein the coating is a gold vapor deposited coating on a chromium priming.

43 ~~179.~~ The device according to claim ~~119~~ 1 wherein two microscope optics facing each other enclose the measuring volume.

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Sub G6 180. The device according to claim 119, further comprising an electrophoretic device with at least one electrophoresis cell having at least one opening for charging/discharging of a sample to be analyzed or of a washing solution, a wall electrode, a ring electrode, a Neher capillary, an electrode at the tip of the capillary and a droplet outlet.

45 ~~181~~. The device according to claim ~~180~~ 44 comprising an electric trap having a quadrupole element with at least four electrodes.

46 ~~182~~. The device according to claim ~~181~~ 45 the quadrupole element includes pin electrodes or vapor-deposited electrodes in a water configuration wherein a hole of < 1mm is lined.

E4 47 ~~183~~. The device according to claim ~~181~~ 45 further comprising at least two additional electrodes in at least a sextupole arrangement .

48 ~~184~~. The device according to claim ~~183~~ 47 wherein the quadrupole element is provided with alternating voltage and a direct voltage is applied to the sextupole electrodes such that the polarity thereof is opposed to the charge of the molecules to be analyzed.

Sub G7 185. The device according to claim 180 characterized in that a sheet for receiving samples is used having specific binding properties for molecules due to molecular derivatization.

50 ~~186~~. The device according to claim ~~185~~ 49 wherein the molecular derivatization includes ion-exchange ligands or affinity ligands.

51 ~~187~~. The device according to claim ~~186~~ 50 wherein said ligands are oligopeptides, polypeptides, proteins, antibodies or chelating agents, especially iminodiacetic acid or nitriloacetic acid ligands.

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sub G8

188. The device according to claim 185 characterized in that sheets are used having different molecular structures of different binding specificity as ligands in specific positions.

189. The device according to claim 180 wherein the sample volume is fixed on a sample receiving device which is two-or three-dimensionally controllable.

190. The device according to claim 189 wherein the sample can be fixed in defined space coordinates with respect to the measuring optics by using two- or three-dimensional piezo drives.

55 ~~191~~. The device according to claim ~~180~~ 44 wherein said device is equipped with an appliance which deflects the laser beam in defined coordinates.

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56 ~~192~~. The device according to claim ~~180~~ 44 wherein said device is equipped with an appliance which can definitely determine the positioning of focusing.

sub G9

193. The device according to claim 119 comprising a multiarray detector.

194. The device according to claim 119 comprising an optical system for the parallel illumination of several excitation volumes.

195. The device according to claim 154 wherein the focused laser beams are being separably arranged halfway between the two ends at the faces of the second supporting arm.

196. The device according to claim 154 wherein the optical elements for the laser beams are arranged at the inner sides, facing each other, of the two holding devices and the optical elements for the fluorescence radiation are arranged at the outer sides, facing away from each other, of the two holding devices.

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197. The device according to claim 154 wherein one of the focusing objective lenses can be positioned by an adjusting element for compensation of an offset of the focuses of said focusing objective lenses.

115 ~~198.~~ The device according to claim 114 ~~197~~ wherein the adjusting element is piezoelectrically driven.

79 ~~199.~~ The device according to claim 60 ~~120~~ wherein the observation unit has photon counting appliances, a correlation appliance, and a multichannel scaler appliance.

sub G10 200. The device according to claim 199 comprising means for processing or evaluating the measuring signal in a computer assisted way.

201. The device according to claim 144 wherein the appliances for prefocusing are provided with a lens and an array corresponding to microscope optics wherein a colonnaded laser beam is focused on the image plane B_1 by a lens and on the image plane B_2 (first image) by said array.

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71 ~~202.~~ The device according to claim 70 ~~201~~ wherein said array is provided with an exchangeable arrangement of lenses for the variation of the diameter of the prefocused laser beam.

81 ~~203.~~ The device according to claim 60 ~~120~~ wherein a detection unit is constituted by two detectors with a beam splitter partitioning the light emitted from the sample to the detectors.

82 ~~204.~~ The device according to claim 81 ~~203~~ wherein the emitted light beam passes imaging lenses and filter elements prior to each of the detectors.

83 ~~205.~~ The device according to claim 81 ~~203~~ wherein the detectors detect light of different wavelengths.

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206. The device according to claim 120 wherein one or more detector elements are placed in the image plane in the form of a detector array.

84 ~~207~~. The device according to claim ~~120~~ 60 comprising two objectives which form an angle of > 90° between them.

sub G11

208. The device according to claim 120 wherein continuous lasers emitting light of wavelengths > 200 nm are used.

209. The device according to claim 208 wherein argon, krypton, helium-neon, or helium-cadmium lasers are used.

210. The device according to claim 120 wherein lasers pulsed with high frequency of ≥ 20 MHz with a power of ≥ 0.5 mW are used.

E4

88 ~~211~~. The device according to claim ~~120~~ 60 wherein appliances for single photon counting are arranged in the beam path of emitted light for detecting the emitted light wherein signal analysis is performed by a digital correlator or multichannel correlator.

89 ~~212~~. The device according to claim ~~211~~ 88 wherein said appliances for single photon counting are avalanche diode detectors.

90 ~~213~~. The device according to claim ~~211~~ 88 wherein said appliances for single photon counting are arranged in the plane of the pinhole aperture.

91 ~~214~~. The device according to claim ~~120~~ 60 wherein the measuring volume is situated in a sample volume between two capillaries, said capillaries being provided with a chemically inert conductive coating at the outer side, and wherein the conductive coatings are connected via

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a computer controlled rectified field or an alternating field and are conductively connected with each other through the measuring volume.

92 ~~215~~. The device according to claim 91 ~~214~~ wherein the coating is a metal vapor deposited coating.

93 ~~216~~. The device according to claim 92 ~~215~~ wherein the coating is a gold vapor deposited coating on a chromium priming.

94 ~~217~~. The device according to claim 60 ~~120~~ wherein two microscope optics facing each other enclose the measuring volume.

sub 6,12

E4

~~218. The device according to claim 120, further comprising an electrophoretic device with at least one electrophoresis cell having at least one opening for charging/discharging of a sample to be analyzed or of a washing solution, a wall electrode, a ring electrode, a Neher capillary, an electrode at the tip of the capillary and a droplet outlet.~~

96 ~~219~~. The device according to claim 95 ~~218~~ comprising an electric trap having a quadrupole element with at least four electrodes.

97 ~~220~~. The device according to claim 96 ~~219~~ the quadrupole element includes pin electrodes or vapor-deposited electrodes in a water configuration wherein a hole of < 1mm is lined.

98 ~~221~~. The device according to claim 96 ~~219~~ further comprising at least two additional electrodes in at least a sextupole arrangement .

99 ~~222~~. The device according to claim 98 ~~221~~ wherein the quadrupole element is provided with alternating voltage and a direct voltage is applied to the sextupole electrodes such that the polarity thereof is opposed to the charge of the molecules to be analyzed.

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Sub G 13

223. The device according to claim 218 characterized in that a sheet for receiving samples is used having specific binding properties for molecules due to molecular derivatization.

101 ~~224~~. The device according to claim 100 ~~223~~ wherein the molecular derivatization includes ion-exchange ligands or affinity ligands.

102 ~~225~~. The device according to claim 101 ~~224~~ wherein said ligands are oligopeptides, polypeptides, proteins, antibodies or chelating agents, especially iminodiacetic acid or nitriloacetic acid ligands.

Sub G14

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226. The device according to claim 223 characterized in that sheets are used having different molecular structures of different binding specificity as ligands in specific positions.

227. The device according to claim 218 wherein the sample volume is fixed on a sample receiving device which is two-or three-dimensionally controllable.

228. The device according to claim 227 wherein the sample can be fixed in defined space coordinates with respect to the measuring optics by using two- or three-dimensional piezo drives.

106 ~~229~~. The device according to claim 95 ~~218~~ wherein said device is equipped with an appliance which deflects the laser beam in defined coordinates.

107 ~~230~~. The device according to claim 95 ~~218~~ wherein said device is equipped with an appliance which can definitely determine the positioning of focusing.

Sub G15

231. The device according to claim 120 comprising a multiarray detector.

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232. The device according to claim 120 comprising an optical system for the parallel illumination of several excitation volumes.

233. The device according to claim 137 wherein the focused laser beams are being separably arranged halfway between the two ends at the faces of the second supporting arm.

234. The device according to claim 137 wherein the optical elements for the laser beams are arranged at the inner sides, facing each other, of the two holding devices and the optical elements for the fluorescence radiation are arranged at the outer sides, facing away from each other, of the two holding devices.

235. The device according to claim 137 wherein one of the focusing objective lenses can be positioned by an adjusting element for compensation of an offset of the focuses of said focusing objective lenses.

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236. The device according to claim 235 wherein the adjusting element is piezoelectrically driven.

237. The device according to claim 155 wherein the focused laser beams are being separably arranged halfway between the two ends at the faces of the second supporting arm.

238. The device according to claim 155 wherein the optical elements for the laser beams are arranged at the inner sides, facing each other, of the two holding devices and the optical elements for the fluorescence radiation are arranged at the outer sides, facing away from each other, of the two holding devices.

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